Antipsychotics, mood stabilisers, and reductions in violence

Corbis

Published Online
May 8, 2014
http://dx.doi.org/10.1016/S0140-6736(14)60694-2

See Articles page 1206

In the past 25 years, evidence has accumulated that people with schizophrenia are at increased risk to commit violent crimes and, to a lesser degree, non-violent crimes compared with the general population.[1] A smaller amount of evidence suggests that patients with bipolar disorder are also at increased risk of committing violent offences.[2] Although both disorders are mainly treated with drugs that reduce risk of relapse, the effect of antipsychotic medications and mood stabilisers on violence has been unclear. In view of the human suffering, stigma, and costs resulting from violence by people with these disorders, the identification of humane and effective strategies to reduce such behaviours is an urgent unmet need.

In their study in *The Lancet,* Seena Fazel and colleagues[3] used Swedish national registers to investigate whether prescriptions for antipsychotic drugs and mood stabilisers were associated with reductions in violent crime. During 2006–09, antipsychotics or mood stabilisers were prescribed to 40 937 men and 41 710 women in Sweden, of whom 2657 (6·5%) men and 604 (1·4%) women were convicted of a violent crime during the study period. Within-individual analyses were used to compare convictions for violent crime during periods when drugs were prescribed compared with periods when no prescriptions were dispensed. Violent crime was reduced by 45% in patients receiving antipsychotics (hazard ratio [HR] 0·55, 95% CI 0·47–0·64) and by 24% in patients prescribed mood stabilisers (0·76, 0·62–0·93). Depot medications (HR adjusted for concomitant oral drugs 0·60, 95% CI 0·39–0·92) and higher doses of antipsychotics were also associated with reductions in violent crime (p=0·019).

Similar reductions in the risk of violent crime were recorded in people with diagnoses of schizophrenia who were prescribed antipsychotic drugs, and in men, but not women, with diagnoses of bipolar disorder who were prescribed mood stabilisers. However, about 60% of the patients prescribed antipsychotics or mood stabilisers did not have diagnoses of schizophrenia, bipolar disorder, or other psychoses. Despite this finding, the reductions in violent crime during periods when medications were dispensed were detected in analyses that included all people prescribed these drugs. These results might represent the increased risk of violent behaviour in people with psychotic-like experiences who do not have psychotic disorders.[4] This issue warrants further investigation.

The study was undertaken carefully, and sensitivity analyses suggest that the results are robust. No age effects were detected in the association between antipsychotics and reductions in violent crime, while the association of mood stabilisers in older patients with bipolar disorder needs further investigation, as do differences in associations in male and female patients. Similar reductions (22–29%) during periods when antipsychotics or mood stabilisers were prescribed were noted for any crime, drug-related crimes, less severe crimes, and suspected violent crimes. Thus, this study provides a basis for future investigations aimed at establishing the type of patient, phase of illness, and type and dose of medication that reduces physically aggressive behaviour. However, many uncertainties remain regarding the treatment of aggression in schizophrenia[5] and bipolar disorder.

In their study, Fazel and colleagues used data from official criminal records of violent crime. However, such criminal records capture only some physically aggressive behaviours, since family members and social and health-care workers—the usual victims—often do not report such behaviours. Methods that ask patients and family and staff to report such behaviours have been shown to be valid.[6] Importantly, in people with schizophrenia the correlates of aggressive behaviour and violent crime are similar.[1] Fazel and colleagues note that randomised controlled trials studying the effect of drug treatments on violence are rare because of low rates of violence. However, when physical aggression towards another is used as the dependent variable, this is not the case. For example, and consistent with previous evidence,[1,6,7] two recent studies that followed patients for 1 year after a first episode of psychosis reported that 38%[8] and 14%[9] of the patients engaged in aggressive behaviour. These rates are sufficiently high to warrant examination of the characteristics of patients who hurt others, and of the effects of drug treatment on such behaviours. These studies identified anger due to delusions[8] and previous antisocial and aggressive behaviour[9] as risk

factors for aggressive behaviour. Therefore, we should ask which antipsychotic drugs can reduce anger caused by delusions. And does the effect of antipsychotics differ depending on the patient's history of violence?

Violent offenders with schizophrenia do not constitute a homogeneous population.[1,5,7] Rather, subtypes of offenders differ by age of onset of antisocial and aggressive behaviour. Those who commit the most offences display a history of such behaviours from childhood and meet criteria for conduct disorder.[1] Men with schizophrenia and previous conduct disorder have been shown to present with changes in grey matter in hypothalamic regions that underlie aggressive behaviour, as do men with previous conduct disorder and no schizophrenia.[10] In the CATIE trial, antipsychotic drugs were not associated with aggressive behaviour of patients with childhood conduct problems.[5,7] In the study by Fazel and colleagues,[3] a trend was noted showing larger reductions in violent crime in people with no previous history of violent crime than in those with previous convictions. This finding is consistent with the notion that individuals with conduct disorder before schizophrenia onset represent a distinct phenotype who may respond differently than other patients to antipsychotic drugs. Another subgroup of patients with schizophrenia begins to engage in aggressive behaviour as illness onsets. It has been suggested that substance misuse might promote this aggressive behaviour.[1] Was the reduction in violent crime associated with antipsychotics and mood stabilisers observed by Fazel and colleagues due to an effect on substance misuse?

During acute episodes of psychosis, when patients are often admitted to hospital against their will, many engage in aggressive behaviour towards others. In most cases, these behaviours disappear within days of administration of antipsychotic drugs. The main correlates of these behaviours are the severity of the positive psychotic symptoms such as hallucinations and delusions.[11] By contrast, the primary correlates of aggressive behaviour in the community are male sex, history of antisocial and aggressive behaviour, and substance misuse.[1,5] Fazel and colleagues studied patients living in the community and noted evidence of reductions of violence when antipsychotic drugs were prescribed. Does this effect depend on the level of positive symptoms as previously suggested?[12] The phase of illness before the first acute episode also warrants investigation since many, if not most, patients with schizophrenia who will offend do so before their first contact with mental health-care services.[13]

Fazel and colleagues' well executed study[3] provides a basis for future clinical studies aiming to establish how antipsychotics and mood stabilisers can be used to reduce aggressive behaviour. The study illustrates again that de-identified data from national registers that were established for administrative reasons can be used by epidemiologists to identify potential strategies to reduce health-related social problems.

Sheilagh Hodgins
Département de Psychiatrie, Université de Montréal, CP 6128 Succ Centre-Ville (Pavillon 3050), Montréal, Québec H3C 3J7, Canada; and Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
s.hodgins@umontreal.ca

I declare that I have no competing interests.

1 Hodgins S, Piatosa M, Schiffer B. Violence among people with schizophrenia: phenotypes and neurobiology. *Curr Top Behav Neurosci* 2013; published online Dec 7. DOI:10.1007/7854_2013_259.
2 Fazel S, Lichtenstein P, Grann M, Goodwin GM, Langstrom N. Bipolar disorder and violent crime: new evidence from population-based longitudinal studies and systematic review. *Arch Gen Psychiatry* 2010; **67:** 931–38.
3 Fazel S, Zetterqvist J, Larsson H, Långström N, Lichtenstein P. Antipsychotics, mood stabilisers, and risk of violent crime. *Lancet* 2014; published online May 8. http://dx.doi.org/10.1016/S0140-6736(14)60379-2.
4 Mojtabai R. Psychotic-like experiences and interpersonal violence in the general population. *Soc Psychiatry Psychiatr Epidemiol* 2006; **41:** 183–90.
5 Volavka J, Ctrome L. Pathways to aggression in schizophrenia affect results of treatment. *Schizophr Bull* 2011; **37:** 921–29.
6 Monahan J, ed. Rethinking risk assessment. Oxford: Oxford University Press, 2001.
7 Swanson JW, Van Dorn RA, Swartz MS, Smith A, Elbogen EB, Monahan J. Alternative pathways to violence in persons with schizophrenia: the role of childhood antisocial behavior problems. *Law Hum Behav* 2008; **32:** 228–40.
8 Coid J, Ullrich S, Kallis C, et al. The relationship between delusions and violence: findings from the East London first episode psychosis study. *JAMA Psychiatry* 2013; **70:** 465–71.
9 Winsper C, Singh S, Marwaha S, et al. Pathways to violent behavior during first-episode psychosis. *JAMA Psychiatry* 2013; **70:** 1287–93.
10 Schiffer B, Leygraf N, Muller B, et al. Structural brain alterations associated with schizophrenia preceded by conduct disorder: a common and distinct subtype of schizophrenia? *Schizophr Bull* 2013; **39:** 1115–28.
11 Witt K, van Dorn R, Fazel S. Risk factors for violence in psychosis: systematic review and meta-regression analysis of 110 studies. *PLoS One* 2013; **8:** e55942.
12 Hodgins S, Riaz M. Violence and phases of illness: differential risk and predictors. *Eur Psychiatry* 2011; **26:** 518–24.
13 Wallace C, Mullen PE, Burgess P. Criminal offending in schizophrenia over a 25-year period marked by deinstitutionalization and increasing prevalence of comorbid substance use disorders. *Am J Psychiatry* 2004; **161:** 716–27.